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A Comparative Analysis of Lipid Profile Parameters in Type 2 Diabetes Mellitus Patients Undergoing Statin Therapy in Tarhuna

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Background: Type 2 Diabetes Mellitus (T2DM) is a prevalent metabolic disorder associated with dyslipidemia, which significantly increases the risk of cardiovascular diseases. Statin therapy is commonly prescribed to manage lipid profiles in T2DM patients. However, the comparative efficacy of different statins in this population remains underexplored, particularly in specific regional contexts such as Tarhuna City, Libya.

Aims of the Study: This study aimed to assess and compare lipid profile parameters and glycemic control among patients with T2DM receiving statin therapy in Tarhuna City. Additionally, it sought to evaluate the impact of different statin types and glucose-lowering regimens on lipid and blood glucose levels.

Methods: This cross-sectional study was conducted at the Diabetic Clinic in Tarhuna City, Libya, from May to September 2025. A total of 111 adult patients with T2DM were enrolled and stratified into four groups based on the type of statin therapy received: atorvastatin, simvastatin, rosuvastatin, and other lipid-lowering agents. Lipid parameters (total cholesterol, LDL-C, HDL-C, triglycerides) and glycemic control (fasting blood glucose and HbA1c) were assessed. Statistical analyses were performed using SPSS version 27, employing one-way ANOVA and Chi-square tests to evaluate differences among groups.

Results: The study found no statistically significant differences in lipid profile parameters across the statin groups ($P > 0.05$). However, rosuvastatin was associated with the lowest mean triglyceride levels (152.92 mg/dL). Adverse drug reactions were most prevalent among simvastatin users (61.1%), indicating a potential tolerability issue. In terms of glycemic control, patients receiving combined insulin and metformin therapy exhibited the lowest mean blood glucose levels (154.20 ± 45.30 mg/dL).

Keywords: Type 2 Diabetes Mellitus, Statin Therapy, Lipid Profile, Glycemic Control, Rosuvastatin, Adverse Drug Reactions.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. This pervasive condition often leads to a myriad of complications, significantly impacting patient morbidity and mortality rates globally (Aga *et al.*, 2020; Goyal, 2023). Among these complications, dyslipidemia, a significant cardiovascular risk factor, is highly prevalent in individuals with T2DM, affecting approximately 50% of patients and contributing substantially to macrovascular events (Karale *et al.*, 2019; Rajput *et al.*, 2015). Diabetic dyslipidemia, a particularly atherogenic form, is characterized by elevated serum levels of total cholesterol, triglycerides, or both, alongside reduced

high-density lipoprotein cholesterol (Vohra *et al.*, 2019). This altered lipid profile, even when appearing within normal ranges for non-diabetic individuals, often conceals underlying increases in atherogenic subfractions of low-density lipoprotein and remnant lipoproteins, thereby elevating cardiovascular disease risk (Adiels *et al*., 2006; Vohra *et al*., 2019). The qualitative abnormalities observed include an abundance of large VLDL particles rich in triglycerides, small dense LDL particles, increased triglyceride content in both LDL and HDL, and heightened susceptibility of LDL to oxidation (Vergès, 2005). These specific lipid aberrations are primarily driven by insulin resistance, which is a hallmark of T2DM, leading to a complex interplay of metabolic pathways that promote dysregulation of lipoprotein metabolism (Berthézène, 2002). Consequently, managing dyslipidemia is a critical aspect of comprehensive care for individuals with T2DM, as it plays a pivotal role in mitigating the substantial risk of cardiovascular disease inherent in this population (Vijayaraghavan, 2010). Therefore, the identification and aggressive treatment of lipid abnormalities are crucial components of holistic diabetes management aimed at preventing cardiovascular complications (Patti *et al*., 2019). Given this context, understanding the patterns and prevalence of dyslipidemia in specific regional populations, such as Tarhuna City, becomes essential for tailoring effective treatment strategies and improving patient outcomes (Daya *et al*., 2017). Specifically, the predominant lipid abnormalities observed in individuals with T2DM include elevated serum triglyceride levels and diminished high-density lipoprotein cholesterol levels (Sinha & Kishore, 2019). These lipid disturbances are frequently observed even with optimal glycemic control and are a significant contributor to the heightened atherosclerotic burden in diabetic patients (Taha, 2002).

Statin therapy has revolutionized cardiovascular risk reduction, particularly in high-risk populations like those with T2DM, demonstrating a remarkable ability to reduce cardiovascular events by 25–30% (Law *et al*., 2003). Since their introduction in 1987, statins have become the gold standard for cholesterol-lowering medication (Rizal *et al*., 2017). Their primary mechanism involves inhibiting 3-hydroxy-3-methylglutaryl coenzyme-A reductase, the rate-limiting enzyme in cholesterol biosynthesis, thereby reducing atherogenic low-density lipoprotein cholesterol levels (ML *et al*., 2020). Beyond their lipid-lowering effects, statins also exhibit pleiotropic properties, including anti-inflammatory, immunomodulatory, and even anti-microbial effects, further contributing to their overall cardiovascular protective profile. This robust therapeutic efficacy has led to their widespread recommendation as first-line pharmacotherapy for dyslipidemia in T2DM patients by major medical organizations (Hadi & AlAteeq, 2021; Vergès, 2005). The continuous evolution of statin compounds has provided clinicians with various options, each with distinct pharmacokinetic and pharmacodynamic characteristics, making comparative analyses crucial for optimizing treatment strategies.

METHODS

Study Design and Population

This cross-sectional study was conducted at the Diabetic Clinic in Tarhuna City, Libya, between May and September 2025. A total of 111 adult patients diagnosed with T2DM were enrolled. Patients were stratified into four groups based on the type of lipid-lowering therapy received:

1. **Atorvastatin group** (n = 61)
2. **Simvastatin group** (n = 18)
3. **Rosuvastatin group** (n = 12)
4. **Other lipid-lowering agents group** (n = 20), including fenofibrate, gemfibrozil, and ezetimibe.

Data Collection

Demographic and clinical data, including age, gender, duration of diabetes, type of glucose-lowering therapy, and statin use, were collected. Laboratory analyses were performed to measure lipid parameters (TC, LDL-C, HDL-C, TAG) and glycemic markers (fasting blood glucose and HbA1c). Blood samples were collected under sterile conditions, and biochemical analyses were conducted using validated enzymatic methods and automated analyzers.

Statistical Analysis

Data were entered and analyzed using SPSS version 27. One-way ANOVA was employed to assess differences in lipid profile parameters (total cholesterol, LDL-C, HDL-C, triglycerides) across the four statin therapy groups. This method was appropriate as it allows for the comparison of means among multiple groups. Post-hoc analyses using Tukey's HSD test were conducted to identify specific group differences when ANOVA indicated significant results. Additionally, independent t-tests were used to compare mean blood glucose and HbA1c levels between different glucose-lowering therapy groups. The Chi-square test was employed to examine the association between statin type and the occurrence of adverse drug reactions. Results were reported as mean ± standard deviation (SD), and statistical significance was considered at $P < 0.05$.

Ethical Considerations

Ethical approval was obtained from the relevant institutional review board. Written informed consent was obtained from all participants, and data confidentiality was strictly maintained.

RESULTS

Demographic and Clinical Characteristics

The mean age of the study population was 52.93 ± 16.60 years, with a nearly equal gender distribution (51.4% female, 48.6% male). The majority of patients were on atorvastatin therapy (54.9%), followed by non-statin agents (18.0%), simvastatin (16.2%), and rosuvastatin (10.8%), as illustrated in the following figure.

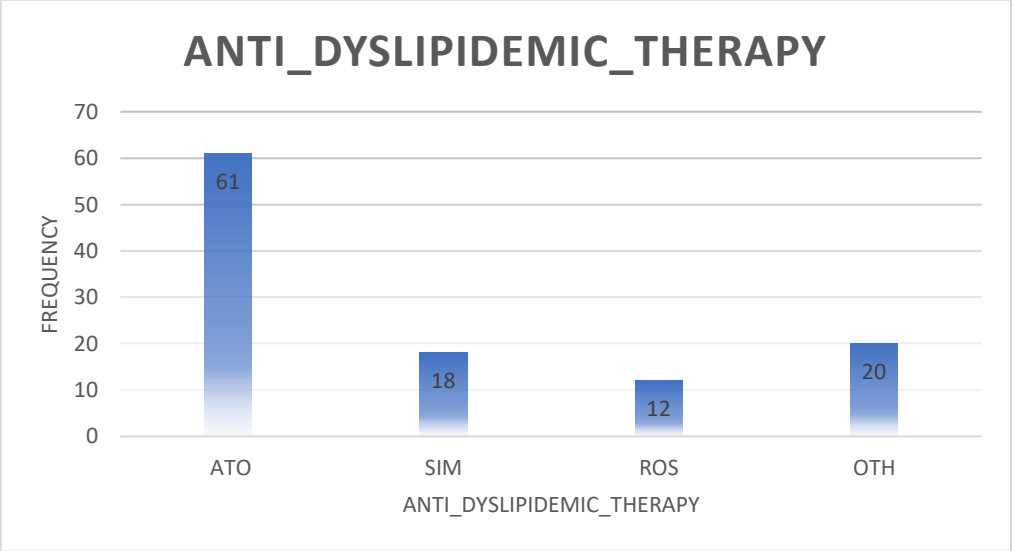

Figure 1: Distribution of Patients by Type of Lipid-Lowering Therapy

Lipid Profile Parameters

No statistically significant differences were observed in TC, LDL-C, HDL-C, or TAG levels across the four statin groups ($P > 0.05$). However, rosuvastatin was associated with the lowest mean TAG level (152.92 ± 52.82 mg/dL), suggesting a potential advantage in managing hypertriglyceridemia, as shown in Table 1.

Table 1: Comparison of Lipid Profile Parameters Among Type 2 Diabetic Patients on Different Statin Therapies

Variables	Therapy	Mean ± SD (mg/dL)	P-value	Homogeneous Subsets
TC	Atorvastatin (n=61)	206.75 ± 44.78	0.879	3[a]
	Simvastatin (n=18)	199.22 ± 49.58		1[a]
	Rosuvastatin (n=12)	200.33 ± 48.37		2[a]
	Other (n=20)	209.85 ± 51.81		4[a]
LDL-C	Atorvastatin	132.71 ± 39.99	0.734	4[a]
	Simvastatin	125.77 ± 54.21		2[a]
	Rosuvastatin	119.78 ± 47.92		1[a]
	Other	124.50 ± 41.51		3[a]
HDL-C	Atorvastatin	47.84 ± 13.00	0.349	1[a]
	Simvastatin	47.88 ± 21.99		1[a]
	Rosuvastatin	53.28 ± 15.63		2[a]

	Other	54.75 ± 21.82		2[a]
TAG	Atorvastatin	202.53 ± 215.48	0.716	4[a]
	Simvastatin	183.89 ± 59.78		3[a]
	Rosuvastatin	152.92 ± 52.82		1[a]
	Other	166.75 ± 40.95		2[a]

Glycemic Control

Among the 111 statin-treated patients with type 2 diabetes attending the Tarhuna Diabetes Center, insulin monotherapy was the most frequently prescribed glucose-lowering regimen, accounting for 49.5% of cases (n = 55). Metformin monotherapy was used in 36.0% (n = 40), while only 14.4% (n = 16) received combined insulin and metformin therapy. This distribution highlights the predominance of insulin-based treatments in clinical practice at the center in Figure 2 below illustrates the frequency of glucose-lowering therapies among the study population.

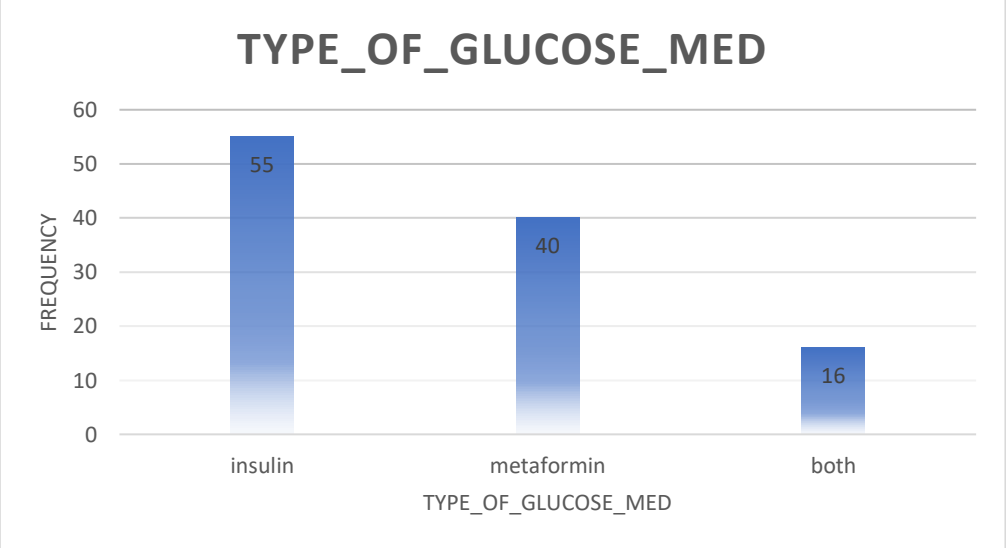

Figure 2 : Distribution of Glucose-Lowering Therapies Among 111 Statin-Treated Type 2 Diabetic Patients

(Bar chart showing: Insulin monotherapy – 55 patients, Metformin monotherapy – 40 patients, Combined therapy – 16 patients)

Despite its limited use, combined insulin and metformin therapy was associated with the lowest mean fasting blood glucose level (154.20 ± 45.30 mg/dL), compared to insulin alone (181.60 ± 71.47 mg/dL) and metformin monotherapy (191.83 ± 62.59 mg/dL). However, no statistically significant differences were observed in HbA1c levels among the three groups (P > 0.05), suggesting comparable long-term glycemic control across treatment modalities. Table 2 below illustrates the mean fasting blood glucose and HbA1c levels across the three treatment groups.

Table 2: Comparison of Fasting Blood Glucose and HbA1c Levels Among Patients Receiving Different Glucose-Lowering Therapies

Type of Glucose Medication	N	Mean Blood Glucose level (mg/dL) ± SD	Mean HbA1c (%) ± SD	Significant Difference in blood Glucose	Significant Difference in HbA1c
Insulin	55	181.60 ± 71.47	8.38 ± 2.18	Yes (vs. Combined therapy)	No
Metformin	40	191.83 ± 62.59	8.08 ± 1.85	No	No
Combined (Insulin + Metformin)	16	154.20 ± 45.30	8.66 ± 1.52	Yes (lower than other groups)	No
Total	111				

Adverse Drug Reactions

Among the various lipid-lowering therapies used in the study, simvastatin was associated with the highest rate of reported adverse drug reactions (61.1%). In contrast, lower rates were observed among patients receiving atorvastatin (27.8%), rosuvastatin (5.6%), and non-statin agents (5.6%). These results indicate a greater incidence of adverse effects among simvastatin users compared to other treatment groups included in the analysis, as illustrated in the following figure.

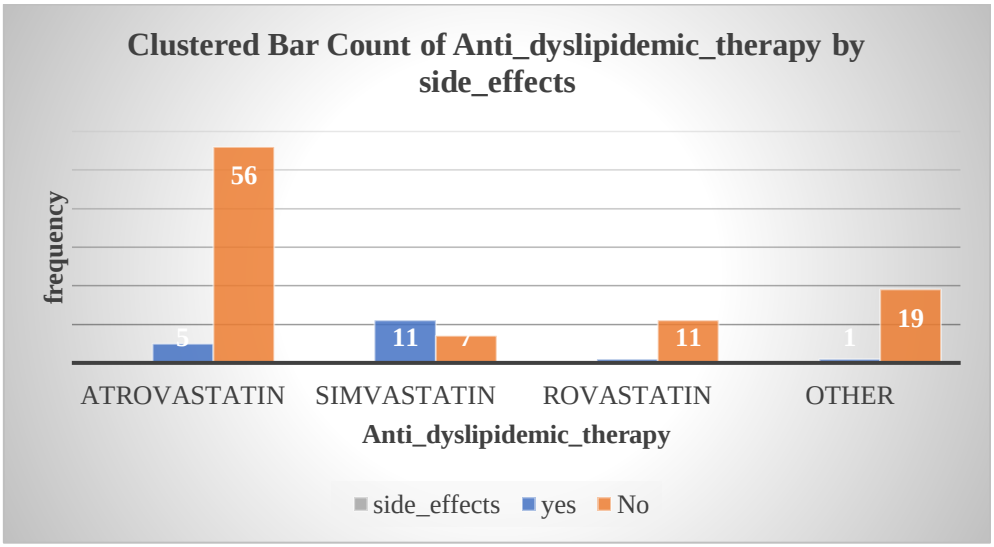

Figure 3: Distribution of Adverse Drug Reactions Across Lipid-Lowering Therapy Groups

DISCUSSION

Comparative Efficacy of Statin Therapies on Lipid Profiles

The present study revealed that all statin therapies—atorvastatin, simvastatin, and rosuvastatin—were effective in maintaining lipid parameters within or near normal reference ranges among patients with type 2 diabetes mellitus (T2DM). Although no statistically significant differences were observed in total cholesterol (TC), LDL-C, or HDL-C levels ($P > 0.05$), rosuvastatin was associated with the lowest mean triglyceride level (152.92 mg/dL), suggesting a potential advantage in managing hypertriglyceridemia.

This observation is consistent with the STELLAR trial, which demonstrated that rosuvastatin had superior efficacy in lowering triglycerides and LDL-C compared to other statins (Jones *et al*., 2003). Its unique pharmacokinetic profile—characterized by high enantioselectivity and minimal CYP3A4 metabolism—may contribute to its enhanced lipid-lowering potency (Climent *et al*., 2021; Luvai *et al*., 2012). Furthermore, rosuvastatin's hydrophilic nature reduces its penetration into extrahepatic tissues, potentially minimizing adverse effects (Pedro-Botet *et al*., 2021). However, the lack of statistical significance in our cohort aligns with findings from the IDEAL study, which reported no major differences in triglyceride reduction between atorvastatin and simvastatin (Pedersen *et al*., 2005). This suggests that while pharmacologic potency varies, patient-specific factors such as adherence, comorbidities, and genetic variability may influence therapeutic outcomes (Rizal *et al*., 2017).

Safety and Adverse Drug Reactions

A striking finding in this study was the significantly higher incidence of adverse drug reactions (ADRs) among patients receiving simvastatin (61.1%), despite its lower prescription rate. In contrast, rosuvastatin and non-statin therapies exhibited the lowest ADR rates (5.6%). These results highlight the importance of tolerability in statin selection, particularly in high-risk populations such as those with T2DM.

Simvastatin's lipophilic nature and extensive metabolism via CYP3A4 increase its susceptibility to drug-drug interactions and myopathy (Schachter, 2004; Thompson *et al*., 2006). This is further supported by pharmacokinetic studies indicating that lipophilic statins diffuse more readily into muscle tissue, potentially triggering muscle-related side effects (Climent *et al*., 2021). Conversely, hydrophilic statins like rosuvastatin rely on active hepatic transport and demonstrate reduced systemic exposure, contributing to their favorable safety profile (Althanoon *et al*., 2020). These findings align with clinical recommendations advocating for cautious use of simvastatin, especially in polypharmacy settings (Pedro-Botet *et al*., 2021). They also reinforce the need for routine monitoring of ADRs and consideration of pharmacogenomic factors when prescribing statins (Mangravite *et al*., 2006).

Glycemic Control and the Role of Combination Therapy

The study's analysis of glycemic control revealed that patients receiving combined insulin and metformin therapy achieved the lowest mean blood glucose levels (154.20 ± 45.30 mg/dL), compared to those on insulin alone (181.60 ± 71.47 mg/dL)

or metformin monotherapy (191.83 ± 62.59 mg/dL). Although HbA1c levels did not differ significantly across groups, the reduction in fasting glucose suggests a synergistic effect of combination therapy. This outcome is supported by the ADA/EASD consensus report, which recommends early use of combination therapy to target multiple pathophysiological mechanisms in T2DM (Davies *et al.*, 2018). Metformin enhances insulin sensitivity and suppresses hepatic glucose production, while insulin directly lowers plasma glucose levels (Nathan *et al.*, 2009). The complementary actions of these agents may explain the superior glycemic outcomes observed. The absence of significant differences in HbA1c could be attributed to variations in treatment duration, adherence, and baseline glycemic status—factors known to influence long-term glycemic markers (Antoniou *et al.*, 2021). Nonetheless, the findings underscore the clinical value of combination therapy in achieving rapid and sustained glucose control, particularly in patients with suboptimal response to monotherapy.

Integrated Management of Dyslipidemia and Hyperglycemia in T2DM

The dual burden of dyslipidemia and hyperglycemia in T2DM necessitates a comprehensive treatment approach. This study reinforces the importance of individualized therapy, where statin selection and glucose-lowering strategies are tailored to patient-specific metabolic profiles. Rosuvastatin's favorable lipid-lowering efficacy and tolerability make it a suitable choice for patients with elevated triglycerides and high cardiovascular risk (Bahar *et al.,* 2023). Meanwhile, the superior glycemic control achieved with insulin-metformin combination therapy supports its use in patients with poor glycemic regulation, aligning with stepwise intensification models (Ji, 2017). Moreover, the interplay between insulin resistance and lipid metabolism—characterized by increased VLDL production, impaired lipoprotein clearance, and elevated free fatty acids—highlights the need for therapies that address both metabolic axes (Chehade *et al.*, 2013; Krauss, 2004). Statins, by improving lipid parameters and exerting anti-inflammatory effects, may indirectly enhance insulin sensitivity and reduce systemic inflammation (ML *et al.*, 2020).

Conclusion

In conclusion, this study provides robust evidence that statin therapies offer comparable efficacy in lipid profile improvement among T2DM patients, with rosuvastatin showing a marginal advantage in triglyceride reduction and tolerability. Simvastatin, despite its lipid-lowering potential, was associated with a higher rate of adverse effects, warranting cautious use. The findings also emphasize the clinical benefit of combination glucose-lowering therapy, particularly insulin plus metformin, in achieving superior glycemic control. These results advocate for a personalized treatment paradigm that integrates lipid and glucose management to reduce cardiovascular risk and improve metabolic outcomes in T2DM. Future research should explore long-term cardiovascular endpoints and incorporate pharmacogenomic profiling to optimize statin and antihyperglycemic therapy selection. Additionally,

larger multicenter studies are needed to validate these findings and guide evidence-based clinical practice in diverse populations.

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